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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/996,128	11/27/2001	Alan N. Houghton	MSK.P-026-3	3698

52334 7590 12/22/2008

Marina Larson & Associates LLC
re: MSK
P. O. BOX 4928
DILLON, CO 80435-4928

EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
12/22/2008	PAPER

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RECORD OF ORAL HEARING

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte ALAN N. HOUGHTON, et al.

Appeal 2008-4425
Application 09/996,128
Technology Center 1600

Oral Hearing Held: November 20, 2008

Before DEMETRA MILLS, LORA GREEN and JEFFREY N. FREDMAN, *Administrative Patent Judges.*

ON BEHALF OF THE APPELLANTS:

MARINA T. LARSON, Ph.D., ESQ.
Marina Larson and Associates, LLC
P.O. Box 4928
330 Dillon Ridge Way
Dillon, Colorado 80435-4928

The above-entitled matter came on for hearing on Thursday, November 20, 2008, commencing at 9:34 a.m., at the U.S. Patent and Trademark Office, 600 Dulany Street, Alexandria, Virginia, before Suzie Dundas, Notary Public.

JUDGE MILLS: Calendar No. 57, Mrs. Larson. Oh, I'm sorry. You have 20 minutes.

DR. LARSON: Obviously this is a case that was briefed way before KSR, so we don't have any the magical words in the case. But it's really a case where the Examiner found the nouns and didn't look a lot at the claims or what the art might have thought about them.

Our claims here are directed to a very specific disease, canine malignant melanoma. Maybe not so important to curing a really tough cancer in people, but it's important. People spend a lot of time and energy on pet animals and money, yes, and the study was actually done because this is such a nasty cancer. If you can treat it in dogs, they're hoping that it will move on to being a very good model for treatment in humans.

The real focus of this work was on the use of xenogeneic antigens. That is, that if you used an antigen from a mouse to treat a human or a human to treat a dog or a mouse to treat a dog, that they were close enough to stimulate an immune response, but not too close. If you're too close, you get the tolerance problem, which is why the body doesn't recognize cancer as evil at all.

So it says "that's just me. I'm not going to fight back." The primary reference, the Zhai reference, does use the xenogeneic antigen. They put a human antigen into a mouse, but the whole purpose in Zhai is to test the effect of the adenoviral vector. They don't attach anything to it being xenogeneic. They use this insipid B-12 lymph melanoma cell line.

Yes, if you select it as in the Nicholson reference that the Examiner relies on, you can make it a bad metastatic cell line. But the one they used is in fact and, as our declaration evidence shows, it probably comes from -- it's

a very old cell line. It's kind of lost in antiquity. But it probably originated from a follicular source, rather than --

JUDGE FREDMAN: Excuse me. I thought it was a B-16 cell line?

DR. LARSON: B-16. I'm sorry, yes. I misspoke. I was thinking vitamins, not melanomas. B-16 was what I meant to say. It's probably follicular in origin, not cutaneous, and therefore it's not a very good model for a mucosa cutaneous cancer like the canine malignant melanoma is.

JUDGE FREDMAN: I was going to ask, the one in Exhibit 4, they would also use B-16 cells.

DR. LARSON: That's right, and it's a very, very common cell line for basic test work.

JUDGE FREDMAN: So your definition says that it doesn't cause metastases, but your spec says, shows that it might immunize with -- and I'm reading from your document (reading from document).

DR. LARSON: Because those were in a test that was specifically designed for doing lung metastases. They were put into the lungs.

JUDGE FREDMAN: Okay.

DR. LARSON: You can convince them to do it --

JUDGE FREDMAN: It says here it was administered subcutaneously and intravenously. It doesn't say that they were put in the lungs. It says (reading from document) subcutaneously, and concurrently with having the compound administered intravenously.

DR. LARSON: Right. But then you're starting to -- you're putting them into the system, in a way to encourage metastases. You can get them to do it. They just don't do it if they don't particularly -- if they're not encouraged to do it. It has no metastatic potential, as opposed to canine

malignant melanoma, which our claims are directed to, which is basically, as the art says, it was considered an incurable disease.

Here we have real honest to goodness data from dogs, where they were doubling their life span, once the disease was detected, and in a couple of cases, at the time that the application was filed, actually had full remissions. And, you know, that's taking animals through an average life of 150 days to over a year. At the time we didn't --- they've had it all, I haven't seen updated data.

But you know, I don't -- it's a significant change. Nothing in this art associates melanoma of the canine type, malignant, with this B-16 cell line. It's just nothing -- we are frequently confronted with the "cancer is too hard to cure. It's too unpredictable. You can't do this, you can't say you're going to cure all kinds of cancer." Yet we then take one effective, you know, a model experiment and say "Oh well, melanoma is melanoma is melanoma." It's just not.

JUDGE FREDMAN: What do you say about the rejection that they say we can support that position? Would you like to support the position in this case, that the melanomas would be different?

DR. LARSON: Well, we have a declaration that says to the extent we understand B-12 or B-16 rather, still on vitamins, it is from a different type of melanoma source. One of the references is basically well, there's melanoma in dogs. Yes, there is. One of our references says there are several kinds of melanoma.

They're the ordinary kind that pop up on the skin that are normally benign, that are quite relatively treatable. Then there are the kinds that are the bad kind, and that's what we're claiming. The kind that's formed up

under the toenails on the nail bed, where you don't see it, and by the time you see it it's gone. It's all over the place. It's, you know, as one article said, "generally incurable."

We're not looking in this application to claim curing melanoma. We're looking at curing a very specific hard to cure melanoma in the independent claim. Now it's important that it be xenogeneic, because when we get down to one of our dependent claims in Claim 30, we say that it's in a non-viral vector, as compared to the adenoviral vector of Zhai.

In the adenoviral vector, the vector acts as an adjuvant. Zhai is testing human materials in an adenoviral vector, and he's using a mouse model. But he's ultimately going to take that human material in the vector and put it into humans. He wants to know if the human, if the adenoviral vector works. He's prepared to assume all the risks that go with being an adenoviral vector, because it does break the tolerance of the immune system.

What the inventors here found, and there's more applications that you may see down the road; when this one was filed, they were not on appeal, is this that you don't need to have a vector that acts as an adjuvant. Just being xenogeneic is enough to break tolerance and to allow the immune system to recognize the tumor antigens, and without kicking off a massive viral immune reaction to the rest of the body.

That's really important. But here, we're only looking at this one disease, you know. We've argued Claim 30 separately. We've argued the claims, the tyrosinase claims separately, and we'd point out that the reference that she relies on as a secondary reference there actually uses the vector in that case to make human melanin in mouse fibroblasts.

JUDGE FREDMAN: She's right about this, that the reaction needs to be suppressed.

DR. LARSON: Oh yes.

JUDGE FREDMAN: Because Zhai mentions tyrosinase directly.

DR. LARSON: Right, no. If the only thing she's citing that for is yes, we know the sequences of the tyrosinase; we know that it can be expressed. But yes, I agree. It's not a biggie. It's not a large problem to enable. But to go from that to say use that system that we used to make melanin to generate antigens to treat an incurable disease is just too much of a leap. It's not common sense. It doesn't -- there is no motivation. There is no predictability. It doesn't follow any of the tests for a case of prima facie obviousness. There's no expectation --

JUDGE FREDMAN: Isn't there a reference in Zhai that teaches that xenogeneic treatments cure at least some melanoma?

DR. LARSON: No. Zhai teaches that an antigen in an adenoviral vector, where the antigen just happens to be xenogeneic. But if you read Zhai, the entire focus of the reference is on the vector and its ability to act as an adjuvant.

JUDGE FREDMAN: Zhai agrees with the results on the left.

DR. LARSON: Oh he did, absolutely. But in that vector, he would have gotten a result with syngeneic materials.

JUDGE FREDMAN: That would be speculating.

DR. LARSON: He would, because he's going to take that vector and that human antigen and put it into people. That's the next step. He's not interested in treating cancer in mice. I think we can take that as a given. You don't want to. But he ends his paper by saying, discussing the problems

with adenoviral vectors, and then says "Despite these toxicities, recombinant adenoviral vectors containing TAAs have many advantages, including a broad range of infection, etcetera. Adenovirus-based tumor vaccines thus appear to be good candidates."

He doesn't say anything about the fact that this is xenogeneic. So if we were dealing with an anticipation rejection, which we're not here, because there's nothing in here about canine malignant melanoma, yes. The other claims we have narrowed the claim in the other application, where we are on a broader scope on melanoma, we have limited the claims to non-viral vectors and argued that extensively.

Here, we're only interested in this one generally incurable disease. It's not mentioned anywhere in any of the references, other than it happens to be a form of melanoma, which is a little bit like saying it's cancer that occurs in certain places.

JUDGE FREDMAN: I think you mentioned that this was about dogs.

DR. LARSON: Well that's true, but we also have a reference that's cited in the brief, that there were, you know, that says that dogs get melanoma. But they get two kinds of melanoma. They get easy melanoma and hard melanoma.

JUDGE MILLS: Does the art recognize this canine malignant melanoma as limited to a specific strain? I'm not sure I read that here. Do people of ordinary skill in the art understand we're only talking about --

DR. LARSON: Yes, absolutely. There's a number of exhibits attached there which relate to the art. As we quoted in, there's several quoted on page three of the brief. They're referenced. The National Canine Cancer Foundation quote there talks about melanomas that occur in areas of

hair, skin, where they usually form small, dark lumps, but can also be kind of flat. Melanoma of hair in dogs is usually benign.

In contrast, malignant melanoma, which occurs in the mouth or in the distal limbs, usually the toenail beds, is an incurable disease. This is very much a term of art. If you put canine malignant melanoma into Google, you will get back this, not little lumpy bumps that happen out on the body.

JUDGE FREDMAN: You expect they'll talk about the CMM.

DR. LARSON: Right. Very specific. It's in the mouth; it's in -- up in the toenails, and it's a death sentence. And being just about to get two new puppies to carry on the generation, you know, I was very happy my dogs made it to 15 years. But I can't imagine would I would go through. This is a really specific case, and it's important that when we do focus our claims, we don't keep getting the same arguments, saying "Oh well yeah, but melanoma is melanoma is melanoma."

But we know that's not true. We can just look at John McCain, who's had it three times, and it's a disease that, you know, in that condition other people have died.

JUDGE FREDMAN: I'm sure that's true in humans, that there are multiple kinds of melanomas.

DR. LARSON: Yes, and there's multiple kinds in dogs, too. That's the evidence that's quoted on page three.

JUDGE MILLS: It didn't look like that was the only rejection that we had in the case, and I think we understand your positions. Was there anything else you'd like to add?

DR. LARSON: Nope.

JUDGE MILLS: Okay, very good.

DR. LARSON: Not unless you want to see pictures of the puppies. They're little. They're four weeks old.

(Whereupon at 9:50 a.m., the oral hearing was adjourned.)